REMARKS

Favorable reconsideration of the present application is respectfully requested in view of the above amendments and the following remarks. Claims 1-4, 8-26, and 30-41 are currently pending and under consideration. Applicants have amended claims 20 and 40 to more particularly point out and distinctly claim certain embodiments of Applicants' invention. Support for the amended claim is provided throughout the specification, including, *e.g.*, at page 31, lines 4-25. No new subject matter has been added.

REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH (ENABLEMENT)

The Office Action rejects claims 1-4, 8-26, and 30-41 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Specifically, the Action asserts that the specification does not reasonably provide enablement for expression constructs (or host cells containing them or methods of using them) that do not express the ANT polypeptides as fusion proteins with an N-terminal polypeptide sequence.

Applicants respectfully traverse these rejections and submit that as disclosed in the present specification and recited in the instant claims, Applicants fully enabled the claimed invention at the time the application was filed. Applicants' invention is directed to a recombinant expression construct comprising at least one regulated promoter operably linked to a first nucleic acid encoding a polypeptide having at least 95% identity to a human adenine translocator polypeptide 3 (ANT3) polypeptide comprising the amino acid sequence set forth in SEQ ID NO:33, and to related compositions and methods. In another embodiment, the invention is directed, in pertinent part, to a recombinant expression construct comprising at least one regulated promoter operably linked to a nucleic acid molecule comprising a first nucleic acid sequence that encodes a polypeptide having at least 95% identity to a human ANT3 polypeptide (SEQ ID NO:33), and a second nucleic acid sequence, wherein the ANT3 polypeptide is expressed as a fusion protein with a polypeptide product of the second nucleic acid sequence, and to related compositions and methods.

Applicants submit, contrary to the PTO's assertions, that the instant claims are commensurate in scope with the disclosure of the specification and that the specification enables a skilled artisan to make and use, without undue experimentation, the claimed recombinant expression constructs and the related compositions and methods. The specification describes methods for making recombinant full-length human ANT polypeptides using recombinant expression constructs that have a regulated promoter operably linked to the nucleic acid encoding the ANT polypeptide (*see, e.g.,* page 14, lines 21-28; page 15, lines 19-28; pages 61-74 (Example 1)). Thus, for example, according to the specification the nucleic acid may include (i) *only* the coding sequence for the ANT polypeptide (*e.g.,* SEQ ID NOS: 31, 32, or 33); (ii) the *coding sequence* for the ANT polypeptide *and additional coding sequence*; or (iii) *coding sequence* for the ANT polypeptide and *non-coding sequence* (*e.g.,* page 20, lines 14-30; page 23, line 26 through page 24, line 8).

As conceded by the PTO, the specification teaches how to make and use a recombinant expression construct that encodes a fusion protein comprising at least one promoter operably linked to a nucleic acid molecule comprising a first nucleic acid molecule that encodes a first polypeptide and a second nucleic acid molecule that encodes a human ANT3 polypeptide having an amino acid sequence at least 95% identical to SEQ ID NO:33 (*see, e.g.,* page 22, line 22 through page 27, line 29). The specification also teaches that polypeptide sequences, for example, polyhistidine, immunoglobulin constant region, protein A, streptavidin or a GST polypeptide, fused to an ANT polypeptide, may be useful for facilitating detection, localization, and/or isolation of ANT (*see, e.g.,* page 25, lines 12-25; page 26, lines 13-27; *see also* Example 1).

Contrary to the assertion by the PTO, however, the specification is <u>not</u> so limited as to teach that recombinant ANT polypeptide expression in a host cell will be achieved *only* when a recombinant expression construct comprises a nucleotide sequence that encodes non-ANT sequences at the amino terminal end of an ANT polypeptide. The specification thus teaches that such non-ANT sequences useful for purification and isolation may also be fused to the carboxy terminus of an ANT polypeptide (*see, e.g.,* page 25, line 23 through page 26, line 27, including references cited therein; *see, e.g.,* page 5, lines 18-20). These non-ANT polypeptide

sequences, as described in the specification, are well known in the art for use as fusion protein domains, for example, to aid in the isolation and/or purification of a polypeptide of interest (*see, e.g.,* page 25, line 23 through page 27, line 7).

As also noted above, the specification clearly teaches that the subject invention recombinant expression construct may comprise a regulated promoter operably linked to a nucleic acid encoding an ANT polypeptide as recited, *without* the nucleic acid comprising any additional polypeptide encoding sequence. Applicants are somewhat puzzled by the assertion made by the PTO that "undue experimentation would be required to develop recombinant expression of *non-fusion* ANT polypeptides having the claimed sequences that would be active and useful" (Action, at page 6, lines 3-5, emphasis added). Specifically, in Example 4 (pages 83-87 and Figure 10) the specification describes recombinant expression in yeast of human ANT3 polypeptides by themselves, and not as fusion proteins (*see e.g.*, page 86, lines 6-7: " . . . huANT3 produced from the yeast expression constructs lacks an epitope tag . . .").

In view of the foregoing, Applicants disagree with the PTO's assertion that undue experimentation would be required to practice the claimed invention. As just noted, the specification not only provides clear and abundant guidance with regard to how recombinantly to express unmodified ANT polypeptides, but further provides a working example of such an invention embodiment.

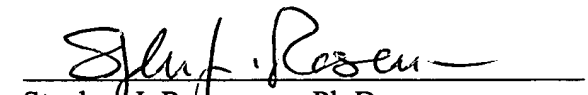
The PTO therefore errs in its assertion that addition to or replacement of human ANT polypeptide specific amino terminal sequences is *required* for expression of an ANT polypeptide in a recombinant expression system, based on the results described in Hatanaka et al. years after the filing date of the present application (*Biol. Pharm. Bull.* 24:595-99 (2001)). Hatanaka et al. were unable to express human ANT (AAC1) specific RNA in the yeast recombinant expression system disclosed therein unless nucleotides encoding human ANT amino terminal amino acids were replaced with nucleotides encoding yeast ANT amino terminal amino acids (*see* Hatanaka et al., Figure 3). Hatanaka et al. did not, however, employ a regulated promoter, which is a feature of the instant claims (see, *e.g.,* Hatanaka et al. at page 598, right-hand column, second paragraph, first sentence; *see also* Applicants' Amendment with Remarks filed on December 4, 2003, of record). By contrast, in the present application Applicants have

provided a working example showing recombinant human ANT expression in a (heterologous) yeast recombinant expression system using a non-fusion construct, *i.e.*, without modifying the ANT-encoding nucleic acid by any addition and/or substitution of nucleotide sequences encoding any amino terminal polypeptide sequence (*see* page 83, line 13 through page 86, line 3).

Applicants therefore respectfully submit that the present specification provides ample guidance enabling a person skilled in the art to make and use the entire breadth of the claimed invention, readily and without undue experimentation. Accordingly, Applicants respectfully submit that the Application satisfies the requirements for enablement under 35 U.S.C. § 112, first paragraph, and request that this rejection be withdrawn.

Applicants respectfully submit that all claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned representative at 206-622-4900.

Respectfully submitted,
SEED Intellectual Property Law Group PLLC



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